

REMARKS

In this paper, claims 1 and 161 are amended. Claim 169 is new. Upon entry of the claim amendments, claims 1-169 are currently pending in this application, of which claims 1, 2, 161-163, and 169 are pending for further examination on the merits, while claims 3-160, and 164-168 are withdrawn.

Claim 1 has been amended for clarification. Specifically, a minor informality has been corrected with respect to the substituent “-BODIPY-FL” as appearing in the definition sections for R_2 , R_3 , and R_4 . Further clarification has been made in the definition sections for the variables “ R_k ” and “ R_j ”. Support for the amendments can be found throughout the specification including the claim as originally presented, for example, lines 5-9, and 11-14 of page 6 of the as-filed specification.

Claim 161 has also been amended for clarification. Support for the amendments can be found in the as-filed claim.

Claim 169 is new. Support for the claim can be found throughout Applicants’ specification including the claim as originally presented, for example, claim 1 as originally filed, and line 13 at page 4 through line 15 of page 6 of the as-filed specification.

No new matter has been introduced by virtue of the within amendments.

The amendment of any claim herein is not to be construed as acquiescence to any of the rejections/objections set forth in the Action, and was done solely to expedite prosecution of the application.

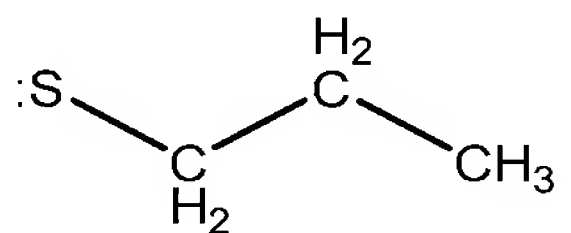
Applicants respectfully reserve the right to pursue any non-elected, cancelled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications. Reconsideration of the application is requested in view of the remarks herein.

Claim Rejection Under 35 USC § 112, Second Paragraph

In the Action, claim 1 (together with dependent claims 2 and 3) is rejected under 35 USC § 112, second paragraph, as allegedly being indefinite. In particular, the Office asserts that the terms “BOPiPy-FL” and “PrS” are vague in meaning; thus, the Office alleges that these terms have rendered the claims indefinite (see page 3 of the Action). Applicants disagree and hereby traverse.

Applicants respectfully submit that one skilled in the art would readily recognize and understand the corresponding structures and scopes thereof which the terms “BODIPY-FL” and “PrS” refer to. Specifically, a skilled artisan would understand that the term “BODIPY-FL” refers to a commonly used molecular fluorophore. The meaning of the term has been widely accepted in the relevant art, as evidenced by the fact that one can readily ascertain its structure (and the synthesis thereof) by searching the term in the literature or through the Internet. Moreover, the term “BODIPY-FL” has been generally understood in the art as corresponding to the trade-name (BODIPY® FL) for the compound “4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diazas-indacene-3-propionic acid”, which is sold commercially by Invitrogen.

Applicants further submit that the term “PrS” stands for a “propyl thio” group. Indeed, a chemist can easily ascertain the meaning and scope of the term, as Pr is a commonly used abbreviation in chemistry for the group “propyl”, while S is ubiquitously used to represent the “sulphur” atom. Thus, Applicants submit that, when being presented with the term “PrS”, a skilled artisan (e.g., a chemist) would readily understand that it stands for chemical structures such as follows:



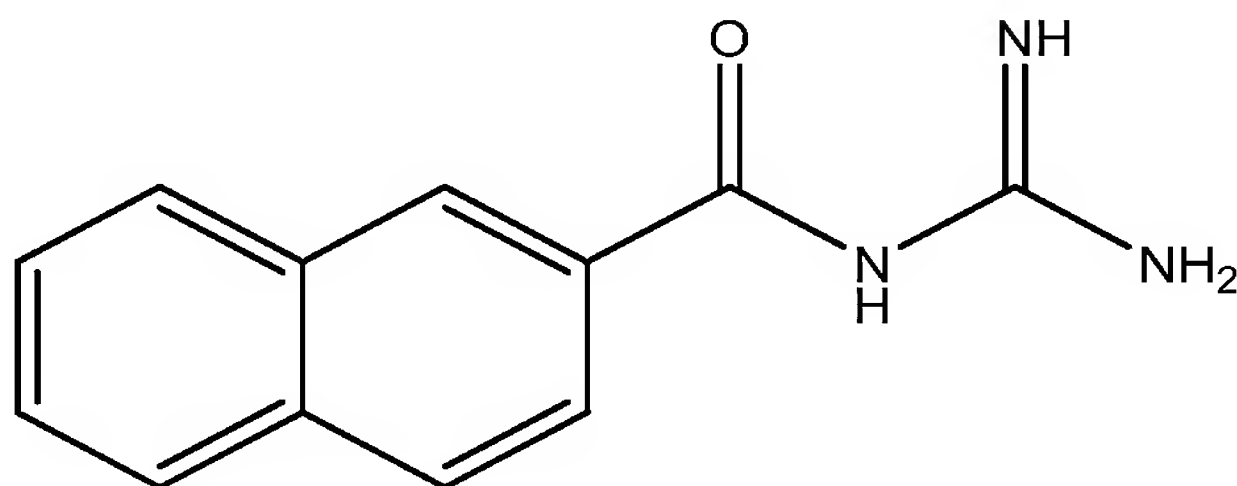
Applicants thus submit that the term “PrS” is clear and definite in meaning, as one ordinary skilled in the art would readily ascertain the meaning and the scope of the term.

In view of the foregoing reasons, one skilled in the art would indeed be able to determine the scope of the claimed invention. Accordingly, Applicants submit that the scope of claim 1 (together with its dependent claims) is clear and definite. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is requested respectfully.

Claim Rejection Under 35 USC § 102

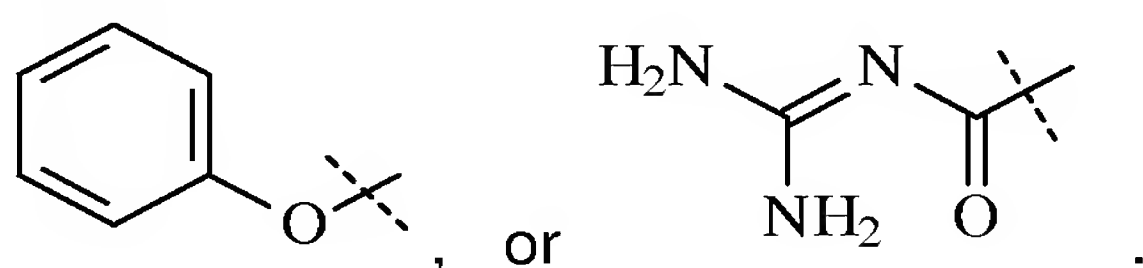
Claims 1 and 161 (together with claims 2, 162 and 163) are rejected under 35 USC § 102(b) as allegedly being anticipated by Yamamoto *et al.* (Chemical & Pharmaceutical Bulletin (1997), 45(8), 1282-1286; hereinafter “Yamamoto”). In

particular, the Office asserts that Formula I in claim 1 has been anticipated by a compound of Yamamoto with the following structure:

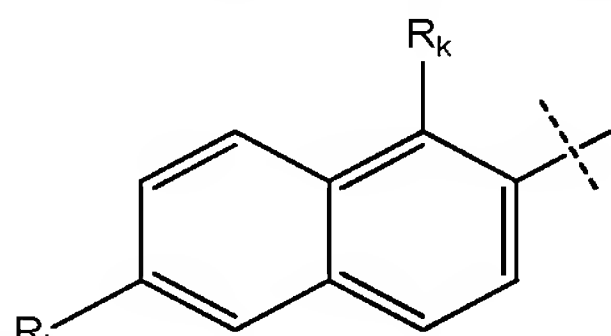


. Applicants hereby traverse.

Nevertheless, without conceding the validity of the Office's assertion and solely for facilitating the prosecution of the present application, the pending claims now recite a compound of Formula I, wherein when R_j is hydrogen, R_k can only be amino, halo, C_{1-5} alkyl, C_{1-5} alkyloxy, hydroxy, aryl, substituted aryl, and etc. , and wherein when R_k is hydrogen, R_j can only be amino, halo, C_{1-5} alkyl, C_{2-5} alkyloxy, hydroxy, aryl, substituted aryl, substituted amino, alkyl-substituted amino, cycloalkyl-substituted amino, aryl-substituted amino, PrS,



(see claims 1 and 169 for detailed definitions). In other words, R_k and R_j cannot both simultaneously be hydrogens in a compound presently claimed. In contrast, applying the definitions of Formula I in the present application, the above cited Yamamoto compound



has R_1 being R_j , with both of R_k and R_j being hydrogens (as commented at page 3 of the Action). Clearly, the compounds of this invention are novel over Yamamoto, as Yamamoto *does not and cannot* anticipate the present Formula I of the application.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. 102(b) of the pending claims is respectfully requested.

Claim Rejection under 35 U.S.C. §103(a)

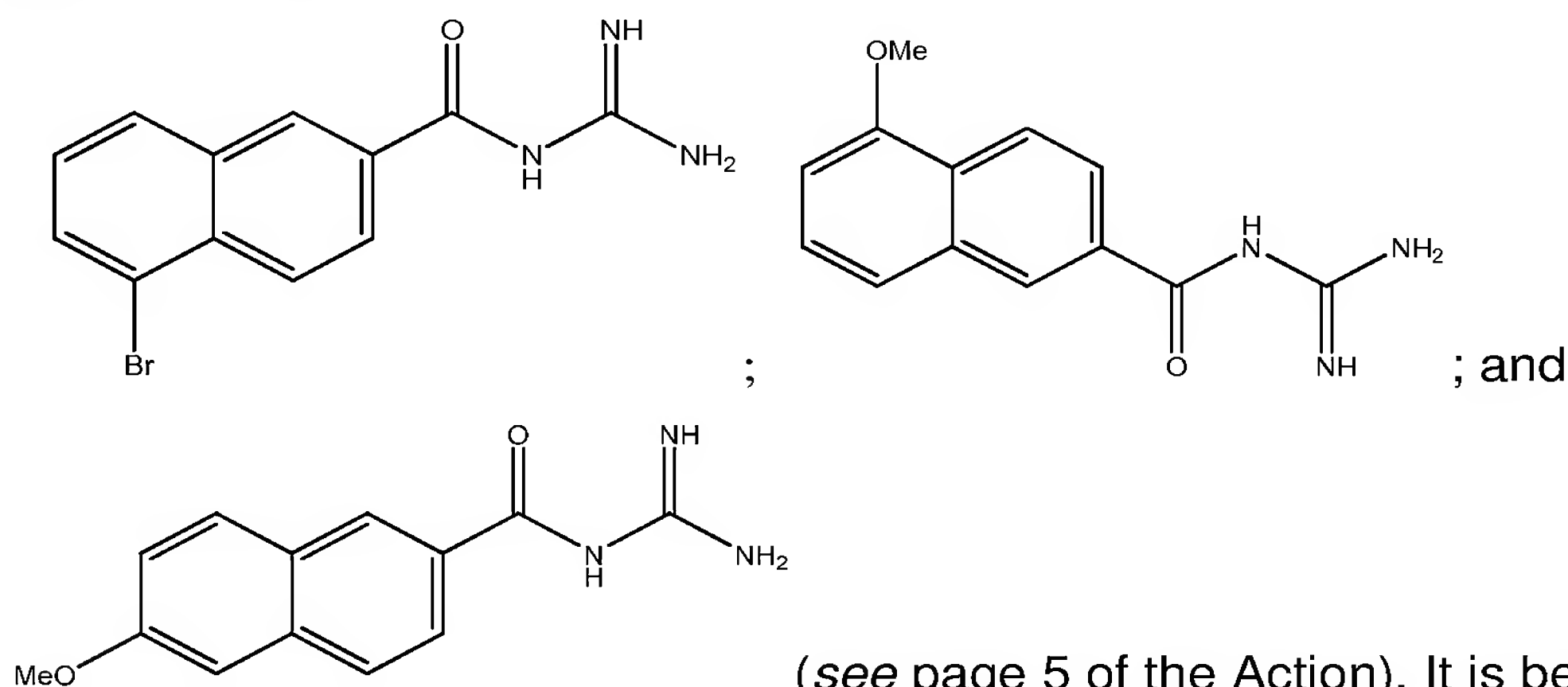
Claims 1 and 161 (together with claims 2, 162 and 163) have been rejected in the Action under 35 U.S.C. §103(a) as allegedly being obvious over Yamamoto. The Action

asserts that Yamamoto discloses a specific compound that falls within the scope of the instant claims, and that it would be obvious to a skilled artisan to arrive at the claimed subject matter through a modification on the Yamamoto compound (see pages 5 and 6 of the Action). Applicants respectfully traverse.

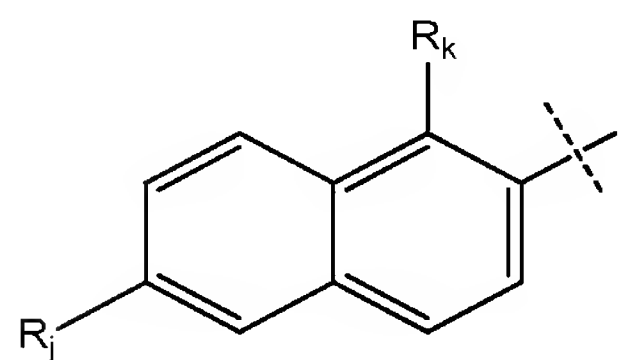
To properly determine a *prima facie* case of obviousness, the Examiner “must step backward in time and into the shoes worn by the hypothetical ‘person of ordinary skill in the art’ when the invention was unknown and just before it was made.” M.P.E.P. § 2142. This is important as “impermissible hindsight must be avoided and the legal conclusion must be gleaned from the prior art.” *Id.* Three criteria may be helpful in determining whether claimed subject matter is obvious under 103(a): first, if there is some suggestion or motivation to modify or combine the cited references; second, if there is a reasonable expectation of success; and third, if the prior art references teach or suggest all the claim limitations. *KSR Int’l Co. v. Teleflex, Inc.* No 04-1350 (U.S. Apr. 30, 2007). With regard to the first criterion, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.3d 690 (Fed. Cir. 1990). “Knowledge in the prior art of every element of a patent claim ... is not of itself sufficient to render claim obvious.” *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1333-34 (Fed. Cir. 2002)]. The issue is whether there is an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *KSR Int’l Co. v. Teleflex, Inc.*

With respect to cases involving new chemical compounds, a *prima facie* case of obviousness requires “that the ‘prior art would have suggested making the specific molecular modification necessary to achieve the claimed invention’”. *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007). The *Takeda* court acknowledged “the importance of identifying ‘a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does’ in an obviousness determination”. *Id.* The issue is whether or not there is a reason “that would have led a chemist to modify a known compound in a *particular manner* to establish *prima facie* obviousness of a new claimed compound”. *Id.*

First of all, Applicants submit that the presently claimed compounds are novel over the Yamamoto disclosure (as above discussed). In addition to the compound discussed in the above section, the Office states that Yamamoto also discloses the following compounds:



(see page 5 of the Action). It is believed that the Office's reasoning in finding the *prima facie* case only applies to the compounds of the present Formula (I), wherein R_1 is a naphthalenyl moiety (that is,



in Formula I of claims 1 and 169).

Applicants contend that a skilled artisan would view the presently claimed compounds patentably different and distinguishable in structure from those disclosed in Yamamoto. Specifically, the presently claimed compounds do not share the same R_1 moiety as the compounds disclosed in Yamamoto. In other words, the R_1 moiety (that is defined and claimed for the compounds of this application) cannot be a naphthalenyl ring having the same substituent(s) at the same position(s) as required for the Yamamoto compounds. It is well understood in the art that different substituents or substitution patterns would potentially have a significant effect on the activity or reactivity of a naphthalenyl ring (and further on the activity/reactivity of the whole molecule). Thus, Applicants submit that a skilled artisan would agree that the compounds of this invention are patentably distinct from the Yamamoto compounds.

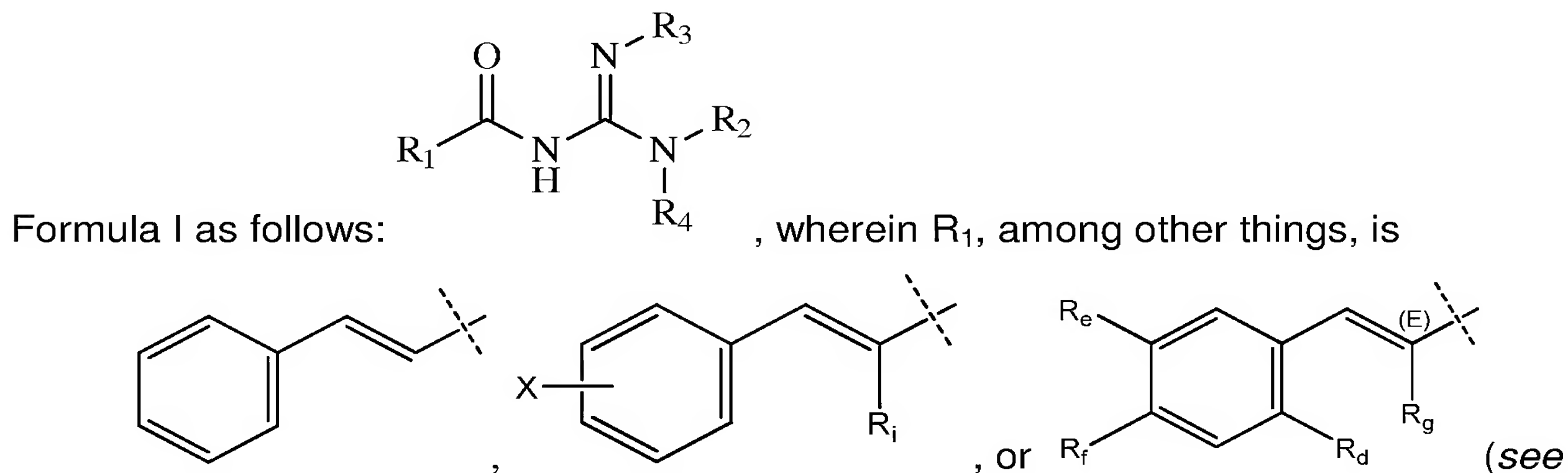
Applicants further note that Yamamoto does not provide any motivation or suggestion to a skilled artisan for modification of its compounds, let alone a specific modification, such as replacement of specific substituents at the specific positions in the Yamamoto compounds that would be required for arriving at the compounds of this

invention. As such, Applicants submit that the Office fails to establish a *prima facie* case of obviousness of the presently claimed subject matter over Yamamoto (especially under the *Takeda* standards).

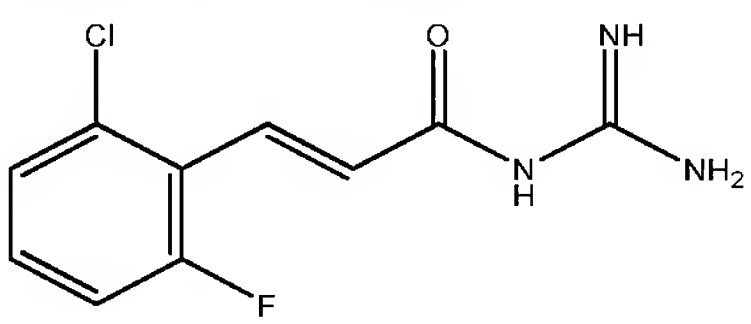
Accordingly, Applicants submit that the claimed subject matter of this application is patentable over Yamamoto. Therefore, reconsideration and withdrawal of the rejection of the pending claims under 35 USC § 103(a) over Yamamoto is respectfully requested.

Claims 1 and 161 (together with claims 2, 162 and 163) have also been rejected in the Action under 35 U.S.C. §103(a) as allegedly obvious over Bream (Arzneimittel-Forschung (1975), 25(10), 1477-82; hereinafter "Bream"). The Action asserts that the presently recited and claimed compounds would be obvious to a skilled artisan through replacing a halogen atom (that is, chlorine) in a Bream compound with a fluorine atom (see page 6 of the Action). Applicants disagree and hereby traverse.

Applicants contend that the presently claimed compounds are patentable over the compounds disclosed in Bream. The present application relates to a compound of



Clearly, Formula I of this application does not

encompass the 2,6-di-substituted compounds (such as, ) as asserted by the Office (see page 6 of the Action). In other words, the difference between the presently claimed compounds and those described in the Bream reference is more than just a replacement of one halogen with another as asserted in the Action. Indeed, the differences between the compounds of this application and those of Bream include *different* substituents at *different* positions even for one portion (that is, the R₁ moiety) out of the whole compound structure. Accordingly, one skilled in the art would agree that

that the presently claimed compounds are patentably different and distinct in structure from those disclosed in Bream.

Applicants further note that Bream does not provide any motivation or suggestion to a skilled artisan to modify its compounds, let alone a significant and specific modification that would be required for arriving at the compounds of this invention. Indeed, in view of the distinct structures the Bream compounds have, those skilled in the art would readily and reasonably expect the Bream compounds to have significant differences in their uses and/or activities from the presently claimed compounds. Applicants thus submit that, based on the Bream disclosure, one skilled in the art would not be motivated to modify the compounds disclosed therein for the purpose to arrive at the presently claimed compounds, let alone with any reasonable expectation of success.

Accordingly, Applicants submit that the claimed subject matter of this application is patentable over Bream. Therefore, reconsideration and withdrawal of the rejection under 35 USC § 103(a) over Bream is respectfully requested.

Moreover, claims 1 and 161 (together with claims 2, 162 and 163) have been rejected in the Action under 35 U.S.C. §103(a) as allegedly obvious over Yamamoto in view of Bream. The Action asserts that the presently recited and claimed compounds would be obvious to a skilled artisan through combining the teachings on various substituents in Yamamoto and Bream (see page 8 of the Action). Applicants respectfully traverse.

Applicants submit that the above reasoning in rebutting the obviousness rejections over Yamamoto or Bream is also applicable in this section of the discussion. As such, Applicants submit that the presently claimed subject matter is patentable over either Yamamoto or Bream.

Applicants further submit that the combination of Yamamoto and Bream still fails in rendering the presently claimed subject matter obvious. As discussed above, Applicants submit that the presently claimed compounds are significantly different and distinguishable in structure from those disclosed in Yamamoto and Bream. And, neither Yamamoto nor Bream provides any motivation or suggestion to a skilled artisan to make a *significant and specific* modification on their compounds (or make a combination of the two) in order to reach the compounds of this invention. Indeed, one ordinary skilled in the art would readily and reasonably expect that the compounds in Yamamoto and

Bream would demonstrate significant differences either in their uses or activities from those claimed in this application, at least due to their distinct structural features. It follows that there is no reasonable expectation of success in the art for one to make a combination of Yamamoto and Bream for arriving at the presently claimed subject matter. As such, Applicants submit that the presently claimed subject matter is patentable over Yamamoto in view of Bream.

Therefore, reconsideration and withdrawal of the rejection under 35 USC § 103(a) over Yamamoto in view of Bream is respectfully requested.

CONCLUSIONS

In view of the above, each of the pending claims in this application is believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call one of Applicant's undersigned representatives to discuss the application. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge any credits or deficiency in the fees filed (or with any paper hereafter filed in the fees filed (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 64681(70403).

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Respectfully submitted,

By /Weiyang Yang/

Jeffrey D. Hsi

Registration No.: 40,024

Weiyang Yang

Registration No.: 61,637

EDWARDS ANGELL PALMER & DODGE
LLP

P.O. Box 55874

Boston, Massachusetts 02205

(617)239-0416

Attorneys/Agents For Applicant